REMARKS

Claims 1-11, 14-17, 19 and 32 are currently pending. For the reasons detailed below, Applicants respectfully request the rejections be withdrawn and the claims be allowed to issue.

The Claims have Sufficient Written Description Support

Claims 1-4, 6-11, and 14-17 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner contends that because Claim 5 depends from Claim 1 and Claim 5 specifically identifies the ATF5 inhibitor of Claim 1 "is selected from the group consisting of ATF5 antibody, siRNA, dominant negative ATF5, and antisense RNA", the genera of inhibitors in Claim 1 is implied to be broader than the recited group in dependent Claim 5. Based on this implication, the Examiner argues that the full scope of such inhibitors is not sufficiently described. Specifically, the Examiner points out that the specification teaches that ATF5 inhibitors may be antibiotics and small molecules, but, allegedly, does not sufficiently describe them to establish possession of those inhibitors at the time the application was filed.

Without acquiescing in the Examiner's position in connection with any implication that may or may not be drawn from the language of Claim 5, Applicants respectfully point out that the instant rejection is improper in light of the species election of May 24, 2007. In particular, Applicants note the inhibitor elected for prosecution on the merits was identified in that species election as dominant negative ATF5. Applicants also point out that, given that election, there can be no implication that the claims currently encompass inhibitors such as

ATF5 antibodies, siRNAs, antisense RNAs, or any other potential ATF5 inhibitor. Accordingly, Applicants respectfully request withdrawal of this rejection.

Furthermore, Applicants assert that notwithstanding the untimeliness of this rejection, the specification does provide a written description of the full scope of Claim 1. The specification provides a number of examples of specific inhibitors of ATF5 and these examples support the broader genus encompassed by Claim 1. The fact that there could be additional species encompassed in that genus does not establish that the support is insufficient. Accordingly, the rejection should be withdrawn.

The Claims Do Not Incorporate "New Matter"

Claim 32 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the Written Description requirement. In particular the Examiner contends that the method described in Claim 32 recites the use of a "fluorescent protein", which encompasses a genus of fluorescent proteins. The Examiner asserts that such a genus includes "new matter" as the specification allegedly only provides support for the use of the species eGFP in such a method. Applicants respectfully traverse this rejection.

In maintaining the instant rejection the Examiner argues that, "as has been long made clear by the courts, obviousness-type support does not provide the proper demonstration of possession under the new matter type of written description rejection."[1] However, Applicants note that the Examiner provides no legal basis for this statement. The Examiner goes on to contend that,

> As has been made abundantly clear in the record, Applicant is not being rejected under the general written description requirement, but instead

[1] See Pending Office Action, Pages 4-5.

> under the new matter type of written description. While a single embodiment in this case may show possession of the genera in an original claim, or in original description, the amended claims are required to have been possessed at the time of filing, which requires more than simple obviousness-type possession.[2]

Again, Applicants note that the Examiner provides no legal basis for this statement. In contrast to the Examiner's contentions, Applicants respectfully submit that the Federal Circuit has indicated that no such alternative standard exists for "new matter type of written description" rejections.

Although non-precedential itself, the Federal Circuit has provided a convenient summary of the precedential case law on this issue in the recent decision in In re Paul Lew and Jason Schiers[3]. In particular, the Federal Circuit in points out:

> we have long explained that the written description requirement of §112 requires the application to "convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991); see also In re Wright, 866 F.2d 422, 424 (Fed. Cir. 1989) ("When the scope of a claim has been changed by amendment in such a way as to justify an assertion that it is directed to a different invention than was the original claim, it is proper to inquire whether the newly claimed subject matter was described in the patent application when filed as the invention of the applicant. That is the essence of the so-called 'description requirement' of §112, first paragraph..."). The claimed subject matter need not be described "in haec verba" in the original specification in order to satisfy the written description requirement. In re Wright, 866 F.2d at 425. Rather, "the test...is whether a person of ordinary skill in the art would recognized that the applicant possessed what is claimed in the later filed application as of the filing date of the earlier filed application." Noelle v. Lederman, 355 F.3d 1343, 1348 (Fed. Cir. 2004). The same standards govern whether new matter has been added to the specification. See Turbocare, 264, F.3d at 1118.[4]

In light of the precedential case law outlined in by the Federal Circuit in the excerpted passage, Applicants respectfully submit that the standard for establishing whether the claimed genus of

[2] Id at Page 5.
[3] In re Paul Lew and Jason Schiers, CAFC 2007-1196, (Fed Cir 2007), copy of slip decision attached.
[4] Id at 5-6, (emphasis in original).

fluorescent proteins is sufficiently described in the specification does not rest on *in haec verba* recitation of alternative species of the genus. Instead, the analysis rests whether one of skill in the art would interpret the specification as identifying the invention as strictly coextensive with the use of the specifically disclosed eGFP species or whether one of skill in the art would recognize that the applicants intended that other species would be equally useful.[5]

In light of the foregoing, the written description requirement for the claimed genus may therefore be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.[6] A "representative number of species" means that the species which are adequately described are representative of the entire genus. Accordingly, in situations where the genus can be adequately described by a single species, that single species is considered a representative number of species.[7] Furthermore, it is well established that "use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description."[8]

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[5] See Phillips v. AWH Corp, 415 F.3d 1303, 1323 (Fed. Cir. 2005) (en banc) (explaining that it will usually be clear from reading the written description whether "the patentee is setting out specific examples of the invention to accomplish these goals, or whether the patentee instead intends for the claims and the embodiments in the specification to be strictly coextensive.")

[6] See Eli Lilly, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

[7] See USPTO Written Description Guidelines, Fed. Reg., Vol. 66, No. 4, pages 1099-1111, 1106 (2001).

[8] See In re Herschler, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteroid in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO)

Applicants note that the instant application describes the auxiliary use of eGFP as a marker throughout the specification, and in particular in Examples, 8-10 (paragraphs [0163] - [0165]). Applicants submit that the functional characteristic of eGFP, specifically, the ability to be used as a marker both at the protein and nucleic acid levels (as described in paragraph [0090]), is equally applicable to the claimed genus of fluorescent proteins. Furthermore, the Examiner has not presented any evidence that the functional recitation of eGFP would be insufficient to lead one of skill in the art to the genus of fluorescent protein markers generally. Finally, Applicants point out that at the time of filing the specification clearly indicated that the examples provided were not intended to be "strictly coextensive" as would be required under the examiner's interpretation by stating that,

> [w]hile the foregoing invention has been described in some detail for purposes of clarity and understanding, it will be appreciated by one skilled in the art, from a reading of the disclosure, that various changes in form and detail can be made without departing from the true scope of the invention in the appended claims.[9]

Accordingly, Applicants respectfully request withdrawal of the instant rejection.

The Claims are Enabled

The Examiner has rejected claims 1-11, 14-17 and 19 under 35 U.S.C. § 112, first paragraph, as lacking enablement. In particular, the Examiner contends that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which it is most nearly connected, to make and/or use the invention. The Examiner contends that the specification is enabling for an *in vitro* method of promoting differentiation of neural stem cells comprising inhibiting ATF5, but does not,

[9] See Paragraph [00204] of the instant application as filed.

according to the Examiner, reasonably provide enablement for an *in vivo* or *ex vivo* method of promoting differentiation of neural stem cells comprising inhibition of ATF5 or transplanting the neural cells into a subject including humans and embryos. The Examiner contends that the claims are unenabled due to the scope of the invention, the state and unpredictability of the art, and the alleged lack of working examples and adequate guidance in the specification.

As outlined in the response filed December 8, 2006, the standard for determining whether claims are sufficiently enabled involves identifying whether the specification provides sufficient guidance that one of skill in the art can practice the invention without undue experimentation.[10] Such a determination involves, but is not limited to, analysis of the following factors: breadth of the claims, nature of the invention, state of the prior art, level of skill of one of ordinary skill in the art, level of predictability, amount of direction provided by the inventor, existence of working examples, and the quantity of experimentation needed to make or use the invention.[11] Applicants also note that under such an analysis, the specification does not need to contain a working example of each embodiment of the invention if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.[12] Furthermore, although a patent application must satisfy the statutory enablement requirements at the time of filing, Applicants point out that additional evidence supporting enablement can be submitted after the application is filed, and can include data generated after the filing date, if that evidence is used "to prove that the disclosure was in fact enabling when filed."[13]

[10] *In re* Wands, 858 F.2d 731 at 737 (Fed. Cir. 1988).
[11] *Id.*
[12] See M.P.E.P. § 2164.02 and *In re* Borkowski, 422 F.2d 904 at 908 (CCPA 1970)
[13] *In re* Brana, 51 F.3d 1560, 1567 (Fed. Cir. 1995).

The instant claims are directed to methods of promoting differentiation of a stem cell or a progenitor cell by inhibiting ATF5 expression. As noted by the Examiner, the instant claims are directed to promotion of differentiation both *in vitro* and *in vivo*.[14] As was also noted by the Examiner, Applicants have disclosed working examples illustrating the suppression of differentiation *in vitro* and the Examiner concedes that *in vitro* methods are fully enabled.[15] Accordingly, the only remaining issue is whether the specification enables promotion of differentiation *in vivo*.

The Examiner's argument suggesting that the specification has not enabled *in vivo* methods centers on the contention that "there are art recognized issues regarding the use of viral vectors that have not been sufficiently addressed by the specification, including potential for immune response to the vector or the gene of interest, limited understanding of likelihood of integration into potential oncogenes, and the ability of animal studies to predict response in humans."[16] The Examiner also suggests that the use of stem cells in medical treatments is not yet developed to a stage where results can be unambiguously predicted.[17] In particular, the Examiner argues that the specification does not provide working examples that would address either of those safety/treatment efficacy issues. Applicants respectfully submit that the standard being applied by the Examiner (that the specification provide working examples that resolve any safety/treatment efficacy issues associated with gene therapy and stem cell therapy) is improper. Since the claims are directed to methods of promoting differentiation via inhibition of ATF5,

[14] See the instant Office Action at Page 6.
[15] Id.
[16] Id. at Pages 7-8.
[17] Id. at Page 8, "The lack of predictability [of the use of stem cells] is found in the areas of: efficacy of stem cell delivery to the area of degeneration, persistence in the disease area and proliferation control...[i]n addition, any neural stem cells that are transplanted into a patient would be under the influence of a myriad number of growth factors, hormones and other molecules that would influence their differentiation fate and efficacy of treatment in any individual case."

Applicants contend that the proper standard requires only that the Applicants establish that the materials and methods disclosed in the specification would allow one of ordinary skill in the art to accomplish such promotion of differentiation *in vivo*, without engaging in undue experimentation. There is no need to establish any sort of safety and/or efficacy profile for treatments based on the materials and methods as is suggested by the Examiner's rejection.

In light of the appropriate standard for determining that the claimed invention is enabled by the specification, Applicants respectfully submit Angelastro *et al.*, J. Neuroscience, 25(15):3889-3899 (2005), which teaches the *in vivo* promotion of neural progenitor cell differentiation using the materials and methods disclosed in the instant specification. In particular, Applicants point to the experiments discussed on pages 3895-3896, which detail the injection of non-replicating retrovirus carrying the dominant negative ATF5 inhibitor gene (Azip-ATF5) into the subventricular zone ("SVZ") of postnatal day 1 rats. These experiments establish that differentiation of SVZ progenitor cells can be promoted by ATF5 inhibition *in vivo*.[18] The methods and materials used in Angelastro *et al.*, are described in detail in the instant application[19] and also find support in the earliest-filed priority document.[20] Accordingly, Applicants respectfully submit that the instant claims are fully enabled by the specification and withdrawal of the instant rejection is requested.

The Claims are Novel

The Examiner has rejected claims 1-3, 7, 12, 14, 16 and 18 under 35 U.S.C. § 102(b) as being anticipated by Angelastro et al. In particular, the Examiner argues that the

[18] See Angelastro *et al.*, Figures 5A and 5B and Page 3896.
[19] See the instant application, paragraphs [0151]-[0156] (methods production of retrovirus containing dominant negative ATF5), [0165] (methods contacting cells with dominant negative ATF5 for *in vivo* contact).
[20] See US Application 60/460,242, paragraphs [0150-154] (methods production of retrovirus containing dominant negative ATF5), [0066]-[0072] and [0098] (methods of contacting cells with inhibitors of ATF5 *in vivo*).

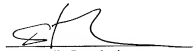
instant specification defines "a specific ATF5 inhibitor" so broadly that the non-specific inhibitor of ATF5 disclosed in Angelastro et al., NGF, is encompassed by that definition, and thus anticipates the claims. Applicants respectfully traverse this rejection.

As pointed out above, Applicants have elected a particular species of ATF5 inhibitor (dominant negative ATF) for prosecution on the merits. In light of this election, and its subsequent impact on the scope of the claims currently under examination, Applicants respectfully submit that the Examiner's contention that the claims encompass non-specific inhibitors is misplaced. Accordingly, Applicants respectfully request withdrawal of the instant rejection.

CONCLUSION

Entry of the foregoing remarks into the file of the above-identified application is respectfully requested. Applicants believe that the invention described and defined by Claim 1-11, 14-17, 19, and 32 are in condition for allowance. Withdrawal of all rejections and reconsideration of the amended claims is requested. An early allowance is earnestly sought.

Respectfully submitted,



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